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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/666,778	09/18/2003	Alain Goossens	2676-6085US	8721

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EXAMINER	
KALLIS, RUSSELL	
ART UNIT	**PAPER NUMBER**
1638	
MAIL DATE	**DELIVERY MODE**
07/31/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/666,778	GOOSSENS ET AL.	
	Examiner	Art Unit	
	Russell Kallis	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 May 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13 and 15-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13,15-19 and 21* is/are rejected.

7)☒ Claim(s) *20* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 20-21 are new. Claims 1-13 and 15-21 are pending and examined.

Rejection of Claim 15 under 35 U.S.C. 102 is withdrawn in view of Applicants amendments.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 21 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 21 recites the limitation "the polynucleotide of SEQ ID NO: 2" in line 2. There is insufficient antecedent basis for this limitation in the claim. SEQ ID NO: 2 is a polypeptide.

Claim Rejections - 35 USC § 103

Claims 1-13 and 16-19 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Theodoulou F. Biochemica et Biophysica Acta; 2000, 1465, pp. 79-103 in view of Dudler R. *et al.* Journal of Biological Chemistry; 25 March 1992, Vol. 267, No. 9 pp. 5582-5888 in further view of Sidler M. *et al.* The Plant Cell, October 1998; Vol. 10, 1623-1636. This rejection is maintained for the reasons of record set forth in the Official action mailed 8/11/2006 and 2/14/2007. Applicant's arguments filed 5/16/2007 have been considered but are not deemed persuasive.

Applicant points to portions of section 5.2 of Theodoulou as evidence that there is no reasonable expectation of success in performing the present invention (response page 8).

Applicant's analysis is misguided. Clearly, the reference teaches transformation of *Arabidopsis* by Sidler *et al.* with the *AtPGP1* encoding an ABC transporter having Walker A and B motifs that is recognized in the art as a nucleotide binding fold gene (see column 2 of Introduction page 1623), where over-expression of *AtPGP1* in transformed plants resulted in around 200 fold greater levels of protein when compared to wild type (see page 1624 column 1 first two full paragraphs especially lines 1-2 of 1st paragraph and last 2 lines of the 2nd paragraph; and figure 1c) that resulted in an increase in hypocotyls length that was strongly correlated with a transport activity of the heterologously expressed *AtPGP1* gene (see). Sidler *et al.* has been added to the rejection to clarify the Examiner's rejection under 103 with respect to Theodoulou. Moreover, it is not clear how Applicant could interpret Theodoulou's statement in section 5.2, which Applicant quotes, "Moreover, the fact that plant secondary products such as vincristin and taxol are often substrates, for or inhibitors of, MDR proteins suggest a role of plant P-gp in synthesis and compartmentation of these compounds", as lack of a reasonable expectation of success, since the claims are drawn to increased secretion (i.e. synthesis and compartmentation). Clearly, Theodoulou and Sidler, incorporated into the teachings of Theodoulou, suggest otherwise.

Applicant asserts that there is no suggestion in Theodoulou *et al.* to motivate one of ordinary skill in the art to use ABC transporter proteins to increase the yield of secondary metabolites in plants and that the combination of Theodoulou and Dudler would require hindsight reasoning (response page 9).

The references as argued supra teach an increased production and/or secretion of a secondary metabolite i.e. the product of the ABC transporter gene (see Sidler page 1629 column 2 1st paragraph of discussion lines 1-8) and one of ordinary skill in the art would have appreciated the usefulness of the ABC transporters.

Applicant submits a declaration from Dr. Alain Goossens showing no effect of non-ABC transporters upon secondary metabolite production. Since the declaration of Alain Goossens is not drawn to any of the species falling within the claimed genus of ABC transport proteins, the declaration will not be given any weight.

In response to applicant's argument that one of ordinary skill in the art would find unexpected the result of an ABC transporter increasing production or secretion of a secondary metabolite; Applicant has demonstrated an induced or enhanced production or secretion of only a nicotine based alkaloid in tobacco transformed with SEQ ID NO: 1. In contrast, the method claims are broadly drawn to a multitude of ABC sequences from a multitude of sources having no specific secondary metabolite specificity, including animal or plant genes encoding ABC transporters; see *In re Lindner*, 173 USPQ 356 (CCPA 1972) and *In re Grasselli*, 218 USPQ 769 (Fed. Cir. 1983) which teach that the evidence of nonobviousness should be commensurate with the scope of the claims. Moreover, Applicant's admission of the state of the prior art in the IDS, specifically WO 98/21938 (Rea) that teaches GS-X as ABC transporter; (see pages 1-6 and 87-89).

The claims are broadly drawn to processes of enhancing secretion of a plant secondary compound by transforming a plant or plant cell with a vector comprising a gene encoding an ABC-transporter; and plants and plant cells thereof.

Theodoulou teaches ABC transporter genes from plants that have strong similarity to MDR proteins from other species and suggests a role of the plant homologues in the secretion or sequestering of *vinca* alkaloid and the alkaloid taxol and suggests a strategy for screening transformed plants and plant cells for determining the specific transport function (section 5.2 page 86).

Dudler teaches an MDR like gene (*AtPGP1*) from Arabidopsis, having nucleotide binding sites (i.e. walker A and B) and transmembrane domains in Figure 6a; and suggests testing to identify substrates (See Abstract and column 1 page 5888 lines 4-7 and 40-53).

Sidler teaches transformation of *Arabidopsis* with the *AtPGP1* gene of Dudler (an ABC transporter having Walker A and B motifs that is recognized in the art as a nucleotide binding fold) where over expression (i.e. secretion to the plasmalemma) resulted in an increase in hypocotyls length (see Abstract; page 1629 column 2 1st paragraph of discussion lines 1-8; and page 1631 column 1 line 28 or 2nd full paragraph); and strongly suggested a transport process (lines 8-9 Abstract).

It would have been obvious at the time of Applicant's filing to take any ABC transporter gene that encoded a protein that had similar structural motifs to the human MRD ABC transporter and test for induced or enhanced production or secretion of any secondary metabolite such as the vinca alkaloid or taxol to determine the function of the plant MDR homologue. One of ordinary skill in the art would have been motivated by the teaching of Theodoulou and by Sidler, that taxol, and other plant secondary metabolites are substrates of or bind to MDR ABC transporter proteins, and would be useful in the art of bioengineering 'secondary product' production and secretion in plants or plant cells that produce taxol, *vinca* alkaloid or other pant

secondary compounds; and have had a reasonable expectation of success given the success of Sidler, that transgenic strategies for evaluating the specific function of plant ABC transporter genes were within the reach of one of ordinary skill and available in the art, and that non-plant alkaloid transporters and methods of transforming plants and maintaining plant cell cultures for the production of secondary metabolites were also known in the art; and wherein screening for vacuolar transport is obvious absent any evidence of criticality.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Claim 20 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Kallis whose telephone number is (571) 272-0798. The examiner can normally be reached on M-F 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on (571) 272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Russell Kallis Ph.D.
July 24, 2007

RUSSELL P. KALLIS, PH.D.
PRIMARY EXAMINER